

PATENT COOPERATION TREATY

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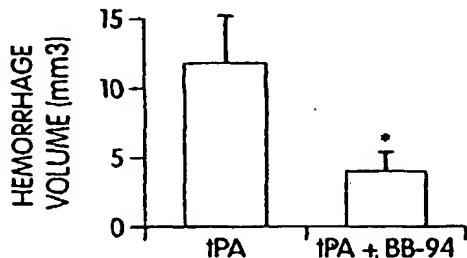
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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

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(54) Title: METHODS AND COMPOSITIONS FOR PROTECTION AGAINST THROMBOLYSIS-ASSOCIATED REPERFUSION INJURY

WO 2004/060293



(57) Abstract: The invention relates to products and methods for reducing cerebral hemorrhage and edema, which can be negative side-effects of thrombolytic therapies with tissue plasminogen activator (tPA) and/or urokinase plasminogen activator (uPA).

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**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US03/40953

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(7) : A01N 37/18  
US CL : 514/2

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
U.S. : 514/2

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
EAST, STN

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	US Pub. No.: US2005/0019329 A1' (Lawerence et al.) 20 May 2003 (20.05.2003), p. 1: [0010]; p. 2: [0021]; p. 3: [0023] and [0026]	1-13, 27-28, and 39-40
X,P	Zhang et al., Circulation. 2002 Aug 6, Vol. 106(6): pp. 740-745, esp. p. 741: column 1, paragraph 2, p. 743: column 2, paragraph 1;	1-3, 5-6, 9-13, 27-28, and 39-40
A	Albers et al., Chest. 2004 Sep; Vol. 126(3 Suppl): pp. 483S-512S	1-13, 27-28, and 39-40

Further documents are listed in the continuation of Box C.

See patent family annex.

Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier application or patent published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means		
"P" document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

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**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US03/40953

**Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)**

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claim Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claim Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
  
3.  Claim Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Continuation Sheet

1.  As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
  
4.  No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: Please See Continuation Sheet

**Remark on Protest**  

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

**INTERNATIONAL SEARCH REPORT**

PCT/US03/40953

**BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING**

1. Claims 1-13, 27-28(in part), 39(in part), and 40, drawn to a method of reducing side effects associated with thrombolytic therapy by blocking tPA binding to LRP.
2. Claims 14-26, 27-28(in part), 39(in part), and 41, drawn to a method of reducing side effects associated with thrombolytic therapy by blocking uPA binding to uPAR.
3. Claims 29-33, drawn to a method of identifying agents that modulate tPA and LRP binding.
4. Claims 34-38, drawn to a method of identifying agents that modulate uPA and uPAR binding.
5. Claims 42-43, drawn to a method of identifying a tPA mutant with decreased binding to LRP.
6. Claims 44-45, drawn to a method of identifying a uPA mutant with decreased binding to uPAR.

This International Searching Authority considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2, and 13.3) for the reason indicated below:

The inventions listing in Groups 1-6 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same corresponding special technical features for the following reasons: The special technical feature of the first claimed invention is inhibiting the binding of tPA and LRP. The feature is not a contribution over the prior art because 39-kD receptor associated protein (RAP) has the ability to inhibit the binding of all ligands, which include tPA, to LRP (Grimsley et al., Thrombosis Research (1997), Vol 88: pp. 458-498, especially s. 486, column 1, paragraph 2). Therefore, there is no special technical feature linking any of the inventions.

**Continuation of Box II Item 4:**

1-13, 27-28 (drawn to tPA/LRP), 39 (drawn to tPA/LRP), and 40

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